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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/020,716	02/09/98	JUNG R	0815

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MARIANNE H MICHEL
PIONEER HI-BRED INTERNATIONAL INC
CORPORATE INTELLECTUAL PROPERTY
7100 NW 62ND AVENUE P O BOX 1000
JOHNSTON IA 50131-1000

EXAMINER
NELSON,A

ART UNIT	PAPER NUMBER
1649	11

DATE MAILED: 11/22/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/020,716	Rudolf Jung, et al.
Examiner	**Group Art Unit**
Amy Nelson	1649

X Responsive to communication(s) filed on *Oct 18, 1999*

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *6, 7, 14-17, and 21-35* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) *6, 7, 14-17, and 21-35* is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____ .

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

X Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- ***SEE OFFICE ACTION ON THE FOLLOWING PAGES*** ---

DETAILED ACTION

Claim Objections

1. The numbering of claims is not accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered Claims 33 and 34 (second occurrence) have been renumbered as Claims 34 and 35.

Claim Rejections - 35 USC § 112

2. Claims 6, 7, 14-17, and 21 remain rejected and new Claims 22-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reasons of record set forth in the last Official action mailed 5/18/99. Applicant's arguments filed 10/18/99 have been fully considered but they are not persuasive.

Applicant asserts that the specification broadly describes rational substitution of amino acids, and provides specific description for hordothionin and ESA. Also, Applicant asserts that the

instant claims are not directed to specific DNA sequences, and hence the Eli Lilly case law is not applicable (response, p. 4-5). Examiner responds that Applicant's description of appropriate substitution of amino acids is limited to the hordothionin protein. Applicant only generally describes amino acid substitution for other proteins, and detailed description with respect to ESA is not provided in the as-filed specification. Further, it is not the claimed subject matter that is relevant in the cited case law, but rather the concept that description of a single species does not adequately describe the genus when no predictions can be made for other members of the genus based on the described species. Therefore, it is maintained that Applicant has not provided appropriate written description of the genus, and it is not clear from the specification that Applicant was in possession of the invention as broadly claimed.

3. Claims 6, 7, 14-17, and 21 remain rejected and new Claims 22-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to transformed cereal plant seed having an elevated lysine, methionine and cysteine content (about 10% to about 35% by weight compared to untransformed cereal plant seed) comprising the modified hordothionin gene of SEQ ID NO:2 (HT12), vectors, plant cells and transformed plants comprising said modified hordothionin gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims. This rejection is repeated for the reasons of

record set forth in the last Official action mailed 5/18/99. Applicant's arguments and the Jung Declaration filed 10/18/99 have been fully considered but they are not persuasive.

Applicant asserts that the instant specification provides guidance for amino acid substitutions in hordothionin and ESA, and that the steps for modeling, modifying and testing hordothionin can be extrapolated to other polypeptides. Furthermore, Applicant asserts that neither full function nor activity are necessary for increased levels of amino acids in the transformed plants (response, p. 5-6). Examiner responds that no specific guidance with respect to ESA is provided in the specification, *i.e.* it is not known how the ESA gene (and hence the encoded ESA protein) is modified by substitution of which amino acids. It is improper to incorporate essential material for practice of the invention by reference, and therefore if appropriate guidance is present in any of the cited references, than the specification must be amended to insert the essential material. The specific guidance provided in the as-filed specification with respect to hordothionin can not be extrapolated to other proteins. One cannot predict the 3-dimensional structure and folding of structurally and functionally unrelated proteins based on the hordothionin protein, and no predictions with respect to the effect of amino acid substitutions (or deletions or insertions) in other proteins can be made based on the disclosed amino acid substitutions in the hordothionin protein. Whereas full function and activity may not be essential for successful increases in designated amino acids, proper protein expression and folding would be required, and phenotypes such as lethality, sterility, or other deleterious effects would necessarily need to be avoided. In view of the unpredictability of gene (and encoded protein)

modification, and of the unpredictability of the phenotype(s) resulting from transgene expression, particularly wherein the transgene is modified from wild type, the successful modification and expression of the hordothionin gene in plants cannot be extrapolated to other genes (and encoded proteins) without additional guidance.

Applicant also argues that detailed guidance for DNA construct preparation are provided for modified hordothionin and ESA genes, and that increased levels of lysine, methionine and cysteine are shown in transformed plants comprising either gene. Applicant argues that one of skill in the art can select plants with the desired phenotype from plants transformed with other genes (response, p. 6-8; Jung Declaration, p. 2-3, Appendices A-C). Examiner responds that, as discussed above, predictions cannot be made with respect to modification of other genes (and encoded proteins) based on the disclosed modifications of the hordothionin gene. Applicant has not provided essential guidance with respect modified ESA genes in the as-filed specification, and incorporation of essential material by reference is improper. Whereas routine experimentation is allowed, the amount of experimentation required to practice the claimed invention with other modified genes constitutes undue trial and error experimentation because Applicant has provided no specific guidance with respect to what amino acids could be substituted without affecting expression and folding of the protein, and without resulting in detrimental phenotypes.

Finally, Applicant asserts that increases in lysine of 31-34.4% are shown in Table 1, and increases in lysine, methionine and cysteine of 10-20% are shown in the Jung Declaration, and therefore Applicant is enabled for the specfically claimed increases (response, p. 8-9; Jung

Declaration, p. 2-3, Appendices A-C). Examiner responds that the instant claims recite increases in up to about 1000%. Such dramatic increases are clearly not supported by the teachings of the specification or of the Jung Declaration.

4. Claims 6, 7, 14-17, 21, and 23-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is dependent on canceled Claim 5.

Claims 7 and 25 are dependent on canceled Claim 1.

Claims 14-17 are dependent on canceled Claim 13.

Claim 21 is dependent on canceled Claim 20.

Claim 23 is dependent on canceled Claim 4.

At Claim 24, line 1, "the plant" lacks proper antecedent basis.

At Claim 25, line 2, the term "derivative" is indefinite. Applicant asserts that the term is clearly defined on page 8 of the Specification to mean a protein that differs from the wild-type protein by "one or more amino acid substitutions, insertions, deletions or the like" (response, p. 10). Examiner responds that the definition reads on essentially any protein, because any protein can be derived by amino acid substitutions, insertions or deletions. Also, it is not known what is intended by "the like." Hence, it is not known what is encompassed by the claim. Appropriate correction is required to clarify the metes and bounds of the claimed invention.

Claim 26 is improperly dependent on Claim 22. It is recommended that the claims be amended to recite --wherein the level of preselected amino acids is at least about 10 percent by weight more than a corresponding untransformed cereal plant seed--.

Claims 27-29 are dependent on canceled Claim 9.

At Claim 30, line 2, the term "elevated" is indefinite because it is not known to what it is compared.

At Claim 31, line 1, the phrase "polypeptide further comprises" does not make sense. Parent Claim 30 does not recite "polypeptide comprises" and hence it is not clear how the polypeptide "further comprises." Appropriate correction is required.

At Claim 31, line 2, the term "elevated" is indefinite because it is not known to what it is compared.

At Claim 32, "seed product" is indefinite. Applicant responds that "seed product" is known in the art and would encompass that containing elevated levels of lysine and a sulfur containing amino acid in the present context (response, p. 11). Examiner responds that it is not known what is encompassed by "seed product" because many different "products" are derived from seeds. Appropriate correction is required to clarify the metes and bounds of the claimed invention.

At Claim 32, "the transformed seed of Claim 22" lacks proper antecedent basis.

At Claim 33, the term "comprising" is unclear in that it is not known what else the seed product comprises. It recommended that the term be changed to --is--.

At Claim 34, the term "express" is indefinite in the present context. Polypeptides are expressed, not amino acids. Hence, it is recommended that the term be changed to --express a polypeptide comprising--.

At Claim 34, line 1, the term "elevated" is indefinite because it is not known to what it is compared.

At Claim 35, line 1, the term "increasing" is indefinite because it is not known to what it is compared.

At Claim 35, "plant cell" at line 2 and "plant" at line 5 are inconsistent with "cereal plant seeds" at line 1. At line 2, "plant cell" should be changed to --cereal plant cell--. At line 5, "plant" should be changed to --cereal plant--.

At Claim 35, line 4, the term "elevated" is indefinite because it is not known to what it is compared.

Claim Rejections - 35 USC § 102

5. Claims 6, 7, 14-17, and 21 remain rejected and new Claims 23 and 25 is rejected under 35 U.S.C. 102(e) as being anticipated by Falco *et al.* (U.S. Patent 5,773,691). This rejection is repeated for the reasons of record set forth in the last Official action mailed 5/18/99. Applicant's arguments filed 10/18/99 have been fully considered but they are not persuasive.

Applicant asserts that the new claims distinguish over the Falco reference (response, p. 12-14). Examiner responds that Claims 6, 7, 14-17, and 21 have not been amended, and therefore are

still anticipated by the disclosure of Falco. Falco also teaches increases in threonine (see abstract), and hence anticipates Claim 23. In view of the indefiniteness of "derivative" in Claim 25, the claim reads on essentially any protein, and hence is anticipated by Falco.

Claim Rejections - 35 USC § 103

6. Claims 6, 7, 14-17, and 21 remain rejected and new Claims 22-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falco *et al.* (U.S. Patent 5,773,691) and Rao (U.S. Patent 5,885,802).

The claimed invention is indefinite for the reasons discussed *supra.*

Falco discloses transformed maize plants and seeds (including seed grains, meal and feed) with enhanced lysine content and threonine content, obtained by expression of chimeric genes encoding lysine insensitive enzymes or lysine-rich proteins (Abstract; Col. 1, lines 18-65; Col. 6, line 22 - Col. 7, line 44; Col. 9, line 38 - Col. 10, line 37; Col. 30, line 15 - Col. 31, line 62; Examples 22, 23, 25). In particular, ~~Applicant~~ Falco teaches said transformed plants wherein the increases in lysine are 10-400% (Col. 6, lines 65-66), and ~~Applicant~~ Falco teaches use of an endosperm-specific promoter, including the zein promoter (Col. 19, lines 40-55).

Rao teaches transformed plants with elevated levels of methionine, a sulfur-containing amino acid, by expression of a mutant barley hordothionin gene with methionine amino acid substitutions (Abstract; Col. 2, lines 19-29; Col. 2, line 66 - Col. 3, line 8). Specifically, Rao teaches transformed cereal crops (Col. 3, lines 55-58).

It would have been *prima facie* obvious at the time of Applicant's invention to combine the methods of Falco and Rao to produce transformed plants and seeds with increases in both lysine and methionine content. One would have been motivated by the teachings of Rao that threonine, lysine and methionine are all essential amino acids required for animal nutrition which are missing from and need to be increased in crop plants (Col. 1, lines 40-42; Col. 2, lines 8-10). One would have had a reasonable expectation of success in view of the success of both Falco and Rao. Applicant has not taught any unexpected results from increasing both methionine and lysine that are nonobvious over a combination of the plants/seeds of Falco and Rao. Therefore, the claimed invention, as broadly claimed, is deemed to be obvious in view of the prior art references.

Applicant asserts that Schernthaner (abstract) and Falco (column 88, lines 37-41) teach away from using the zein promoter (response, p. 15). Schernthaner is not being applied as a secondary reference against the new claims. The cited passage in Falco is directed to the glutelin 2 promoter, and not the zein promoter.

Applicant argues that the new claims distinguish over Rao because the claims recite an increase in both lysine and a sulfur containing amino acid, and because the claims recite endosperm expression (response, p. 15). Examiner responds that the new claims are rejected over both the teachings of Rao and the teachings of Falco, and all of the claim limitations are taught by the combination of the Rao and Falco references.

Applicant asserts that it is inappropriate to use hindsight reconstruction in an obviousness rejection, that there must be reason to combine the references, and that obvious to try does not

constitute obviousness (response, p. 15-16). Examiner responds that the motivation to combine is provided by Rao who teaches that threonine, lysine and methionine are all essential amino acids required for animal nutrition which are missing from and need to be increased in crop plants (Col. 1, lines 40-42; Col. 2, lines 8-10). Hence, it would have been obvious to combine the teachings of Rao and Falco in order to increase both lysine and methionine content. One would have had a reasonable expectation of success in view of the success of both Rao and Falco. Therefore, there would have been not only a motivation to try, but also an expectation of success.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy J. Nelson whose telephone number is (703) 306-3218. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application, or if the examiner cannot be reached as indicated above, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Amy Nelson

AMY NELSON
PATENT EXAMINER

Amy J. Nelson, Ph.D.
November 18, 1999